Croonian Lecture.—*The Physiological Basis of Thirst.*

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A custom which has usually been respected by investigators who in years past have had the high honour of delivering the Croonian Lecture is that of reporting and interpreting a group of related researches upon which they have been engaged and which they have already made public. That is a custom which I should have been happy to follow on the present occasion if military service had not sharply broken in on my studies months ago and made them seem now very remote and the summarising of them a difficult occupation. And, after all, is it not natural for us as investigators to hold the forward look, to consider the problems before us rather than those that have been solved? May I, therefore, be permitted to bring to your attention some ideas and observations which have not yet been published and which, though incomplete, may prove interesting and suggestive.

In regarding the human body as a self-regulating organisation we observe that, so far as mere existence is concerned, it depends on three necessary supplies from the outer world,—on food, to provide for growth and repair and to yield energy for internal activities and the maintenance of body heat; on oxygen, to serve the oxidative processes essential to life; and on water, as the medium in which occur all the chemical changes of the body. These three supplies are of different orders of urgency. Thus a man may live for 30 or 40 days without taking food, as professional fasters have demonstrated,* and suffer no apparent permanent injury to his bodily structure or functions. On the other hand, lack of oxygen for only a brief period may result in unconsciousness and death. Indeed, certain nerve cells in the cerebral cortex cannot withstand total deprivation of oxygen for more than 8 or 9 minutes without undergoing such fundamental changes that they do not again become normal when they receive their proper supply.† Intermediate between the long survival without food and the very brief survival without oxygen is the period of existence which is possible without water. Records of men who have missed their way in desert regions and who, with no water to drink, have wandered in the scorching heat have proved that they rarely live under these circumstances of struggle and torrid atmosphere for more than three

* Luciani, 'Das Hungern,' Leipzig, 1890.

† See Gomez and Pike, 'Jour. of Exp. Med.,' vol. 11, p. 262 (1909).

days, and many die within 36 hours. An exceptional instance has been reported, of a Mexican, who, lost in the dry plains of the south-western part of the United States, walked, or crept on his hands and knees, between 100 and 150 miles, repeatedly drinking his own excretions, and succeeded, after nearly 7 days wholly without water, in reaching a habitation.* This is a record which, for its conditions, has no parallel. If the thirsting man is not subjected to heat or exertion his life may continue much longer than 7 days. Viterbi, an Italian political prisoner, who committed suicide by refusing food and drink, died on the eighteenth day of his voluntary privation. After the third day the pangs of hunger ceased, but, until almost the last, thirst was always more insistent and tormenting. He records again and again his parched mouth and throat, his burning thirst, his ardent and continual thirst, his thirst constant and ever more intolerable.† Thus though the period of survival varies, death is sure to come whether food, or oxygen, or water is withheld.

Normally these three supplies—food, oxygen, and water—are maintained in more or less constant adjustment to the bodily needs. Food material is being continually utilised in building body structure, and in providing energy for bodily activities, but it is periodically restored. Oxygen is continually combining with carbon and hydrogen and leaving the body in CO_2 and H_2O, but the loss is compensated for with every breath. And water, likewise, is always being discharged in expired air, in secretion from the kidneys, and in the sweat. So great is the escape by way of the lungs and skin alone that it is estimated that approximately 25 per cent. of the heat loss from the body is due to evaporation from these surfaces.‡ This continuous lessening of the water content must be checked by a new supply, or important functions will begin to show signs of need.

The evidence for the absolute necessity of water in our physiological processes requires no elaboration. Water is a universal and essential ingredient of all forms of organisms. Without it life disappears or is latent—the dry seed awakens only on becoming moist. Because we may have it at almost any moment we are likely to overlook its absolute necessity in our lives. Among inhabitants of desert regions, however, water is the central nucleus of thought about which all other ideas revolve; it is an ultimate standard of things, incomparably more stable and more exalted than the gold of civilised commerce, the constantly remembered basis of existence.§ In

* McGee, 'Interstate Med. Jour.,' vol. 13, p. 279 (1906).

† Viterbi, quoted by Bardier, Richet's 'Dictionnaire de Physiologie,' article "Faim," vol. 6, p. 7 (1904).

‡ Gephart and Du Bois, 'Arch. Int. Med.,' vol. 17, p. 902 (1916).

§ McGee, "The Seri Indians," '17th Annual Report of the Bureau of American Ethnology,' p. 181.

our bodies the presence of water as the main constituent of the digestive secretions, its *rôle* in the chemical changes of digestion, its service as a vehicle of absorption, its importance in the composition of blood and lymph, its use, together with other substances, in body fluids as a lubricant, its action in regulating body temperature—these functions need merely to be mentioned to illustrate how water influences every activity which living beings display.

Because water is a fundamental essential to life, and is continually escaping from the body, and because there is consequent need for repeated replenishment of the store, an inquiry into the mechanism of the replenishment is a matter of interest.

That such a mechanism exists is indicated by the fact that all our essential functions, leading to preservation of the individual and of the race, are controlled not through memory and volition, but by insistent sensations and desires. The unpleasant sensation of thirst causes us to drink. Not towards the subjective aspect of these automatic arrangements, however, is the special attention of the physiologist directed. He is primarily concerned with the bodily states which give rise to the sensation. Only when these states and their relations to the needs of the organism are known is the automatic control explained.

About six years ago I called attention to some graphic records of motions of the stomach in man which showed that the sensation of hunger is associated with powerful contractions of the empty or nearly empty organ. And because the hunger pang began to be experienced after the contraction had started, the conclusion was drawn that hunger is not a "general sensation," as was formerly held by physiologists and psychologists, but has its immediate origin in the stomach, and is the direct consequence of the strong contraction.* This conclusion has since been abundantly confirmed by Carlson and his collaborators in observations on themselves and on a man with a gastric fistula.†

Even more imperious than hunger as an insistent and tormenting sensation, accompanied by a dominant impulse which determines our behaviour, is thirst. Indeed, these two experiences—hunger and thirst—are such impelling motives in directing our conduct that from early times they have been used as supreme examples of a strong desire. The ancient prophet spoke of a "hunger and thirst after righteousness" to express the eagerness

* The Harvey Lectures, New York, 1911–1912, p. 130—Cannon: Harvey Lecture, December 16, 1911, "A Consideration of the Nature of Hunger"; also Cannon and Washburn, 'Am. Jour. Physiol.,' vol. 29, p. 441 (1912).

† Carlson, 'Control of Hunger in Health and Disease,' Chicago, 1916.

of his yearning. And the common acquaintance of mankind with the potent demands of hunger and thirst for satisfaction renders these similes easily understood.

In undertaking a discussion of thirst it is necessary at the start to distinguish clearly between the primitive sensation itself and appetite. The same distinction had to be drawn in considering the nature of hunger. The hunger pang is a disagreeable ache or gnawing pain referred to the lower mid-chest region or the epigastrium. Appetite for food, on the other hand, is related to previous experiences which have yielded pleasurable sensations of taste or smell. Thus associations become established between particular edible substances and the delights they convey, with the result that a wish develops that the delights may be renewed. In either circumstance, whether for the satisfaction of appetite or for the satisfaction of hunger, the body is supplied with food.

Similarly in the case of drink, the appetite for this or that peculiar potable substance develops from former experience and from established associations of an agreeable character. We drink not only because we are thirsty, but also because we relish a certain aroma or bouquet, or a peculiar taste, and wish to enjoy it again. In respect to appetite the taking of fluid differs from the taking of food, in that fluid, which leaves the stomach rapidly, may not occasion a sense of satiety as does food, which accumulates in the stomach. In this possibility of continuing pleasurable sensations associated with drinking lie the dangers that arise from the excessive use of beverages. Under normal conditions, however, it is through the satisfaction of appetite for a particular drink, *e.g.*, for tea, or coffee, or light alcoholic beverages, that the body may be supplied with sufficient water for its needs before thirst has had occasion to manifest itself. But just as there is provided, back of the appetite for food, in readiness to become imperious if necessary, the sensation of hunger; so likewise, as a final defence against a too great depletion of the water content of the body, there may appear the urgent and distressing sensation of thirst.

There is a general agreement that thirst is a sensation referred to the mucous lining of the mouth and pharynx, and especially to the root of the tongue and to the palate. McGee, an American geologist of large experience in desert regions, who made numerous observations on sufferers from extreme thirst, has distinguished five stages through which men pass on their way to death from lack of water.* In the first stage there is a feeling of dryness in the mouth and throat, accompanied by a craving for liquid. This is the common experience of normal thirst. The condition

* McGee, 'Interstate Med. Jour.,' vol. 13, p. 279 (1906).

may be alleviated, as everyday practice demonstrates, by a moderate quantity of water, or through exciting a flow of saliva by taking into the mouth fruit acids such as lemon or tomato juice, or by chewing insoluble substances. In the second stage the saliva and mucus in the mouth and throat become scant and sticky. There is a feeling of dry deadness of the mucous membranes. The inbreathed air feels hot. The tongue clings to the teeth or cleaves to the roof of the mouth. A lump seems to rise in the throat, and starts endless swallowing motions to dislodge it. Water and wetness are then exalted as the end of all excellence. Even in this stage the distress can be alleviated by repeatedly sipping and sniffing a few drops of water at a time. "Many prospectors," McGee states, "become artists in mouth moistening, and carry canteens only for this purpose, depending on draughts in camp to supply the general needs of the system." The last three stages described by McGee, in which the eyelids stiffen over eyeballs set in a sightless stare, the distal tongue hardens to a dull weight, and the wretched victim has illusions of lakes and running streams, are too pathological for our present interest.

The fact I wish to emphasise is the persistent dryness of the mouth and throat in thirst. Direct testimony is given by King, a medical officer in a United States Cavalry troop, which for $3\frac{1}{2}$ days was lost without water in the torrid "Llano Estacado" of Texas. He records that, on the third day, salivary and mucous secretions had long been absent, and that mouths and throats were so parched that food, on being chewed, gathered about the teeth and in the palate, and could not be swallowed. "Sugar would not dissolve in the mouth."*

Further evidence of the relation between local dryness of the mouth and throat and the sensation of thirst is found in some of the conditions which bring on the sensation. Breathing hot air free from moisture, prolonged speaking or singing, the repeated chewing of desiccated food, the inhibitory influence of fear and anxiety on salivary secretion, have all been observed to result in dryness of the buccal and pharyngeal mucous membrane and in attendant thirst. On the other hand, conditions arising in regions remote from the mouth and involving a reduction of the general fluid content of the body, such as profuse sweating, the excessive diarrhœa of cholera, the diuresis of diabetes, as well as such losses as occur in hæmorrhage and lactation, are well recognised causes of the same sensation. There appear to be, therefore, both local and general origins of thirst. In correspondence with these observations, two groups of theories have arisen, just as in the

*„King, 'Amer. Jour. Med. Sci.,' vol. 75, p. 404 (1878).

case of hunger—one explaining thirst as a local sensation, the other explaining it as a general and diffuse sensation. These theories require examination.

The view that thirst is a sensation of local origin has had few advocates, and the evidence in its favour is meagre. In 1885 Lepidi-Chioti and Fubini* reported observations on a boy of 17, who, suffering from polyuria, passed from 13 to 15 litres of urine daily. When prevented from drinking for several hours, this youth was tormented by a most distressing thirst, which he referred to the back of the mouth, and at times to the epigastrium. The observers tried the effect of brushing the back of the mouth with a weak solution of cocaine. Scarcely was the application completed before the troublesome sensation wholly ceased, and the patient remained comfortable from 15 to 35 minutes. If, instead of cocaine, water was used to brush over the mucous membranes, thirst was relieved for only two minutes. The temporary abolition of a persistent thirst by use of a local anæsthetic, in a human being who could testify regarding his experience, is suggestive support for the local origin of the sensation. The evidence adduced by Valenti is also suggestive. He cocainised the back of the mouth and the upper œsophagus of dogs which had been deprived of water for several days, and noted that they then refused to drink.† One might suppose that the refusal to take water was due to inhibition of the swallowing reflex by anæsthetisation of the pharyngeal mucosa, as reported by Wassilief.‡ But Valenti states that his animals are quite capable of swallowing.§

Though these observations are indicative of a local source of the thirst sensation, they leave unexplained the manner in which the sensation arises. Valenti has put forward the idea that all the afferent nerves of the upper part of the digestive tube are excitable to stimuli of thirst, but that suggestion does not advance our knowledge so long as we are left unenlightened as to what these stimuli are. A similar criticism may be offered to Luciani's theory that the sensory nerves of the buccal and pharyngeal mucosa are especially sensitive to a diminution of the water-content of the circulating fluid of the body; indeed, that these nerves are advance sentinels, like the skin nerves for pain, warning the body of danger.‖ No special features of the nerves of this region, however, are known. No special end-organs are known. The intimation that these nerves are peculiarly related to a general bodily need is pure hypothesis. That they

* Lepidi-Chioti and Fubini, 'Giorn. d. R. Accad. d. Med.,' Turin, vol. 48, p. 905 (1885).
† Valenti, 'Arch. Ital. de Biol.,' vol. 53, p. 94 (1910).
‡ Wassilief, 'Ztschr. f. Biol.,' vol. 24, p. 40 (1888).
§ Valenti, 'Cbl. f. Physiol.,' vol. 20, p. 450 (1906).
‖ Luciani, 'Arch. di Fisiol.,' vol. 3, p. 541 (1906).

mediate the sensation of thirst is unquestioned. But the problem again is presented, How are they stimulated ?

The view that thirst is a general sensation was well stated by Schiff. It arises, he declared, from a lessened water-content of the body, a condition from which the whole body suffers. The local reference to the pharynx, like the local reference of hunger to the stomach, is due to association of experiences. Thus the feeling of dryness in the throat, though it accompanies thirst, has only the value of a secondary phenomenon, and bears no deeper relation to the general sensation than heaviness of the eyelids bears to the general sensation of sleepiness.* The conception of thirst, as a general sensation, is commonly accepted, and is supported by considerable experimental evidence. The interpretation of this evidence, however, is open to question, and should be examined critically.

First among the experiments cited are those of Dupuytren and the later similar experiments of Orfila.† These observers abolished thirst in dogs by injecting water and other liquids into the dogs' veins. And Schiff quotes Magendie as having treated successfully by the same procedure the thirst of a patient suffering from hydrophobia. In these instances the treatment was no doubt general, in that it affected the body as a whole. But the assumption that thirst is thus proved to be a general sensation is unwarranted, for the injection of fluid into the circulation may have changed local conditions in the mouth and pharynx, so that the local sensation no longer arose.

A classic experiment repeatedly cited in the literature of thirst was one performed by Claude Bernard. He opened a gastric fistula which he had made in a dog, and allowed the water which the animal drank to pass out. As the animal became thirsty, it would drink until "fatigued," as the report states, and when "rested" it would begin again. But after the fistula was closed, drinking quickly assuaged the desire for water. The inference was drawn that thirst must be a general sensation, for the passage of water through the mouth and pharynx wet those surfaces, and yet the animal was not satisfied until the water was permitted to enter the intestine and be absorbed by the body.‡ This evidence appears conclusive. The expressions "fatigued" and "rested," however, are interpretations of the observer, and not the testimony of the dog. Indeed, we may with equal reasonableness assume that the animal stopped drinking because he was not thirsty, and started again when he became thirsty. The only assumptions necessary for such an interpretation of the animal's behaviour are that appreciable time is

* Schiff, 'Physiologie de la Digestion,' Florence and Turin, vol. 1, p. 41 (1867).

† See 'Dictionnaire des Sci. Méd.,' Paris, vol. 61, p. 469 (1821).

‡ Bernard, 'Physiologie Expérimentale,' Paris, vol. 2, p. 49 (1856).

required to moisten the buccal and pharyngeal mucosa sufficiently to extinguish thirst—a point made by Voit*—and that these regions become dried rapidly when there is absence of an adequate water-content in the body. This interpretation is consistent with the view that thirst is a sensation having a local source. Furthermore, this interpretation is not contradicted by the satisfaction manifested by the dog after the fistula was closed, for the water which is absorbed, like that injected into veins, may quench thirst by altering local conditions. We cannot admit, therefore, that Bernard's experiment is proof that thirst is a general sensation.

Another set of observations cited as favourable to the theory of the diffused character of the origin of thirst are those of Longet. After severing the glosso-pharyngeal, the lingual and the vagus nerves on both sides in dogs, he observed that they drank as usual after eating.† If thirst has a local origin in the mouth and pharynx, why should the animals in which the nerves to these regions were cut still take water? Two answers to this question may be given. First, as Voit has pointed out,‡ Longet did not cut all branches of the vagi and trigemini to the mouth and pharynx, and, consequently, some sensation persisted. And second, even if all nerves were cut, the fact that the animals drank would not prove that thirst exists as a general feeling, for one may drink from the sight of fluid, or from custom, without the stimulation of a dry mouth, just as one may eat from the sight of food without the stimulus of hunger. In other words, the element of appetite, previously considered, may enter, and as a matter of habit and associated experience determine present reactions.

The remaining evidence in favour of the diffused origin of thirst is found in studies of blood changes. These changes, by altering the "milieu intérieur" of the body cells, must affect them all. In 1900, Mayer published reports on the increase of osmotic pressure of the blood, as determined by depression of the freezing point of the serum, which he noted in conditions naturally accompanied by thirst. Dogs deprived of water for several days had a blood serum in which the osmotic pressure was increased, and rabbits kept in a specially warmed chamber showed the same change. Thus, conditions in which the water supply to the body was stopped, or the loss of water from the body by sweating or pulmonary evaporation was increased, either of which is known to cause thirst, were associated with a rise of osmotic pressure. And Mayer argued that all other circumstances in which thirst appears—in diabetes with increased blood sugar, in renal disease with

* Voit, 'Hermann's Handbuch der Physiologie,' Leipzig, Abth. 6, p. 566 (1881).

† Longet, 'Traité de Physiologie,' Paris, vol. 1, p. 35 *et seq.* (1868).

‡ Voit, *loc. cit.*

accumulation of waste material in the body fluids, in acute rabies with total deprivation of water, in cholera with excessive outpouring of water into the intestine—the osmotic pressure of the blood would be augmented. Moreover, when a thirsty dog drinks, the hypertonicity of his serum disappears, his normal condition is restored, and he stops drinking.

By these observations Mayer was led to the conclusion that whenever the osmotic pressure of the blood rises above normal, thirst appears; whenever it returns to normal, thirst vanishes; and as the pressure varies, thirst also varies. Since intravenous injections of hypertonic salt solution cause, by stimulation of the bulbar centres, according to Mayer, a rise of arterial pressure and renal and intestinal vasodilation—both operating to lower the abnormally high osmotic pressure of the blood—he infers that other agencies are present in the organism besides the desire for water, which tend to keep the blood normal. Thirst, he declares, is the last of a series of mechanisms acting to protect the organism against hypertonicity of its fluids.

In summary, then, the thirsty individual has a blood with high osmotic pressure. This condition affects all the cells of the body. It disturbs the cells of the central nervous system, and thus leads both to protective circulatory reactions and, in case these fail, to malaise and irritability, and a reference of unpleasantness to the region of the pharynx. Accompanying this, there is the impulse to drink, and when that is satisfied, the water taken in restores the normal state.*

Mayer's observations were soon confirmed, but his inferences were challenged. In 1901, Wettendorff, working in Brussels, reported that if dogs are deprived of water their blood does, indeed, develop a hypertonicity, as Mayer had found, but that this is a phenomenon which does not occur to any marked degree in the first days of the deprivation. In one instance there was no change in the freezing point of the serum during three days of thirst. Serious alteration of the osmotic pressure of the blood, therefore, is comparatively tardy in its appearance. Since the organism is continually losing water, and, nevertheless, the blood remains for a day or two unchanged, Wettendorff concluded that the consistency of the blood is preserved as long as possible by withdrawal of water from the extravascular fluids and the tissues. Further, thirst is clearly demonstrable long before any considerable change in the blood is evident. One animal in which the freezing point of the serum had been lowered only 0·01° C. by four days' deprivation of water, drank 200 c.c. of physiological salt solution, a liquid which to the dog in normal condition is quite repugnant. Again, when the blood has become

* Mayer, 'C. R. Soc. de Biol.,' vol. 52, pp. 154, 389, 522 (1900); also 'Essai sur la Soif,' from the Laboratory of Experimental Pathology, Faculty of Medicine, Paris, 1900.

slightly hypertonic, a dog may drink normal salt solution without lowering his osmotic pressure and afterwards, by refusing further drink, act quite as if he had slaked his thirst. But if an animal with a very hypertonic blood is placed before hypertonic salt solution he takes it again and again—an action which may be explained by a draining of water from the tissues with increasing intensity, and a consequent increasing thirst.

From all these observations Wettendorff concluded that the origin of thirst does not reside in alterations of the blood itself, but in the act of withdrawing water from the tissues. The liquids bathing the cells, therefore, would be first to concentrate as water is lost from the organism. And since the conditions of cellular life would thus be modified in all the tissues, the peculiar state would develop which occasions the sensation of thirst. This effect is generally diffused, and is independent of any peculiar influence of the process of dehydration on the nervous system itself.

In accounting for the localising of the sensation in the mouth and throat Wettendorff distinguished between a "true thirst" and a "false thirst." "True thirst," he declared, is dependent on an actual bodily need, and is persistent until the need is satisfied. "False thirst" is only a dryness of the mouth and pharynx. Dryness in this region occurs, to be sure, in true thirst, but it is then an expression of the general dehydration of the tissues, exaggerated perhaps by contact with the outer air. Through experience the two conditions—buccal dryness and general dehydration—have become associated. Even in true thirst we may temporarily abolish the sensation by moistening the pharyngeal mucous membrane, but the result is only a "false satisfaction," a self-deception, made possible because long and pleasant experience has proved that moistening this region by drink leads to the satisfaction of an instinctive need.*

The foregoing review of observations and theories has revealed that the attitude of physiologists with reference to thirst has been much as it was with reference to hunger. In each condition a general bodily need has arisen from a lack of essential bodily material and is signalled by a well-defined sensation. In each the testimony of ingenuous persons regarding their feelings has been carefully set down, and then explained away. Thus in the case of thirst the primary sensation is described universally as an experience of dryness and stickiness in the mouth and throat.† Instead of attempting to account for the experience as such,

* Wettendorf, 'Travaux du Laboratoire de l'Institut Solvay,' Brussels, vol. 4, pp. 353–484 (1901).

† Foster, 'Textbook of Physiology,' London, p. 1423 (1891); Ludwig, 'Lehrbuch der Physiologie,' vol. 2, p. 586; Voit, 'Hermann's Handbuch der Physiologie,' Abth. 6, p. 566.

however, attention has been paid to the bodily need which accompanies it; apparently, since the need is a general one, the sensation has been supposed to be general, and the thirst which everybody experiences and knows about has been classed as an associated secondary phenomenon or the peripheral reference of a central change. The really doubtful feature in this view of thirst, just as in the older conception of hunger, is the "general sensation." That even the early stages of a need of water may be accompanied by increased irritability, and a vague sense of weakness and limpness, is not denied. But the thirsty man does not complain of these general conditions. He is tormented by a parched and burning throat, and any explanation of the physiological mechanism for maintaining the water content of the body must take into account this prominent fact.

In looking for a mechanism which would automatically keep up the water supply of our bodily economy, we may follow two clues; first, that there may be a peripheral arrangement which in the presence of a general bodily need for water would lead to dryness of the mouth and throat; and second, that a peripheral arrangement of this nature should be especially characteristic of animals which are constantly and rapidly losing water and require repeated renewal of the supply. These two clues offer a biological approach to the explanation of thirst which I wish to utilise.

In one sense all animals are constantly losing water, for even in the simplest forms waste material is excreted in solution. With respect to water loss, however, we should expect to find a marked difference between animals living in water itself and those living in air. Indeed, it is difficult to conceive of an animal living in water as experiencing thirst. The entire body surface and the mouth and throat are throughout active life continuously bathed in a moving flow. The food is taken wet from a wet medium. Probably renal activity and the secretion of the digestive glands are the only important ways for water to leave the economy; and the digestive secretions are soon largely re-absorbed. In contrast, the land animals, mammals, for example, lose moisture not only in these ways but also by the moistening of dry food, by evaporation from the extensive surface of the lungs, and by the action of innumerable sweat glands. It is because of the possibility of great and rapid loss of water from its body that the land animal has special need for an assurance of adequate supply.

In the water inhabitant the skin, and the mouth and gullet, are all kept wet by the medium in which he lives and moves. In the process of evolution, however, as organisms changed their habitat from water to air, the skin became dry and scaly. Of the parts which in marine animals were constantly bathed by water, only the mouth and throat continue to be moist. These

regions are now exposed to air, however, instead of being flushed by a flowing stream, and consequently they tend to dry. The structural lining of these parts probably renders them especially liable to desiccation in the presence of dry air, for the mucosa of the mouth and also of the pharynx, below the level of the floor of the nasal chambers, is composed of squamous epithelium. Some scattered mucous glands are present, but they are not capable of keeping the surfaces satisfactorily wet, as any one can readily prove by breathing through the mouth for only a few minutes. When air passes to and fro by way of this watercourse, as in prolonged speaking or singing, and in smoking, it is to be expected, therefore, that feelings of dryness and stickiness, which we call thirst, should arise.

Contrast this condition of the mouth with the condition of the respiratory tract, in which the lining membrane consists of columnar epithelium and is richly provided, particularly in the nose, with multitudes of mucous glands. Through this tract air moves to and fro constantly with no sign of inducing desiccation except in extreme and prolonged deprivation of water. But there is one portion of this normal pathway for the air which, in the absence of sufficient moisture, is peculiarly liable to become dried. It is the pharynx, where the respiratory tract crosses the digestive tract—*i.e.*, where the inbreathed air, which may be insufficiently moistened in the nose, passes over surfaces of the ancient watercourse. Here, even with nasal respiration, unpleasant feelings may be excited, if the water-content of the body is reduced, and, in cases of marked thirst, the dryness of this region may stimulate tireless swallowing motions.

The central questions now appear: Why do not the mouth and pharynx feel dry and uncomfortable under normal conditions? and why do they feel so when the body stands in need of water? Again, a comparison of conditions in the water inhabitants, in which the buccal and pharyngeal regions are kept moistened by the surrounding medium, with conditions in the air inhabitants, in which these regions tend to be dried by the surrounding medium, will offer pertinent suggestions. A characteristic difference between these two animal groups is the possession, by the air inhabitants, of special buccal glands. They are not present in fishes, but are found in the rest of the vertebrate series from the amphibia onwards. At first little differentiated, they develop in mammals into the three pairs of salivary glands—the parotid, sub-maxillary, and sub-lingual. For the purpose of considering thirst in man, we may deal solely with this salivary group. The action of these organs is to secrete a fluid which is normally more than 97 per cent., and may be more than 99 per cent., water.* The

* Becker and Ludwig, 'Ztschr. f. Rat. Med.,' vol. 1, p. 278 (1851).

theory of thirst, on which I wish to offer evidence, may now be stated. In brief, it is that the salivary glands have, among their functions, that of keeping moist the ancient watercourse; that they, like other tissues, suffer when water is lacking in the body—a lack especially important for them, however, because their secretion is almost wholly water, and that, when these glands fail to provide sufficient fluid to moisten the mouth and throat, the local discomfort and unpleasantness which result constitute the feeling of thirst.

That one of the uses of buccal glands is to keep wet the surfaces over which their secretion is distributed is indicated by the fact that these structures first appear in air-inhabiting vertebrates. This indication receives support from the conditions seen in the cetacea, the mammalian forms which have returned to an aquatic existence, and in which both the water-loss from the body and the need for wetting the mouth and throat are greatly reduced. It is a remarkable fact that in these animals the salivary glands are either lacking or are very rudimentary. The appearance and disappearance of the buccal glands in large animal groups, in correspondence with the exposure or non-exposure of the mouth and throat to desiccating air, point to these glands as protectors of the buccal mucosa against drying.

Experimental evidence as to the protective function of the salivary secretions was provided incidentally many years ago by Bidder and Schmidt. They were interested in studying any fluid secretion which might appear in the mouth apart from saliva. To this end they tied in dogs all the salivary ducts. The first effect was such a striking diminution of the fluid layer over the buccal mucosa that only when the mouth was held closed was the surface kept moist, and, when the animal breathed through the mouth, a real drying of the surface was hardly prevented. The eagerness for water, they state, was enormously increased, so that the animal was always ready to drink.*

Related to this service of saliva in moistening and lubricating the mouth parts is the presence of a special reflex for salivary secretion when the buccal mucosa is exposed to conditions which tend to dry it. Thus, as Pavlov's† researches demonstrated, with dry food in the mouth, much more saliva is secreted than with moist food. And Zebrowski‡ found, in the course of observations on patients with a parotid fistula, that, whereas no saliva flowed with the mouth closed, as much as 0·25 c.c. in five minutes came from the duct when the mouth was opened. This reflex is readily

* Bidder and Schmidt, 'Verdauungssäfte und Stoffwechsel,' Leipzig, p. 3 (1852).

† Pavlov, 'The Work of the Digestive Glands,' London, 2nd ed., pp. 70, 82 (1910).

‡ Zebrowski, 'Arch. f. d. ges. Physiol.,' vol. 110, p. 105 (1905).

demonstrated. If one closes the nostrils and breathes through the mouth for five minutes, usually nothing happens during the first minute. The mucosa then begins to feel dry, and at once the saliva starts flowing, and continues for the rest of the period. I have thus collected as much as 4·7 c.c. in four minutes. Chewing motions, with the mouth empty, yielded in five minutes only about 1 c.c. In these observations precautions were taken against any psychic effect due to interest, by adding long columns of figures during the test. It seems clear, therefore, that if the mouth tends to become dry, the salivary glands are normally stimulated to action, and, if there is sufficient outflow from them, the affected surfaces are moistened. The act of swallowing favours the process, for the fluid is thereby spread backwards on the tongue and wiped down the back wall of the pharynx.

The question whether there is a relation between the existence of water-need in the body and diminished flow of saliva I have examined in two ways —by going without fluid for a considerable period and by profuse sweating, combined with measurements of salivary secretion under uniform stimulation. The method of determining salivary output was that of chewing for five minutes and at a uniform rate a tasteless gum, collecting the saliva which flowed during this period, and measuring its volume. All these observations are best made when one is inactive, and in my experience more nearly uniform results are obtained if one lies quiet during the tests.

The influence on salivary flow of going without fluid for some time may be illustrated by an example. The chewing to evoke salivary action was started at 7 o'clock in the morning, and repeated each hour until 8 o'clock in the evening. A breakfast consisting of a dry cereal preparation was taken between 8 and 9 o'clock, and a luncheon of dry bread between 12 and 1 o'clock. Nothing had been drunk since the previous evening. From the first test at 7 o'clock until 11 there was little change in the output of saliva; the average amount secreted in 5 minutes was 14·1 c.c., with variations between 13 and 16·4 c.c. Then the output began to fall, and at 2 o'clock only 6·4 c.c. was secreted. The average amount for the two observations at 2 and 3 o'clock was 7·7 c.c.—only little more than half that poured out in the morning. Between 3 and 4 o'clock a litre of water was drunk. The effect was soon apparent. At 4 o'clock the output was 15·6 c.c., and during the next 4 hours, in which more water was taken, and a supper with thin soup and other fluid was consumed, the average amount secreted was 14·6 c.c., a figure closely corresponding to the 14·1 c.c. of the morning hours. These results are illustrated graphically in fig. 1. Other tests of this character gave similar results, though there was variation in the rate of decrease in the amounts of saliva secreted.

A similar diminution of the salivary secretion occurs after the loss of water from the body by sweating. In one instance, the loss in about one hour

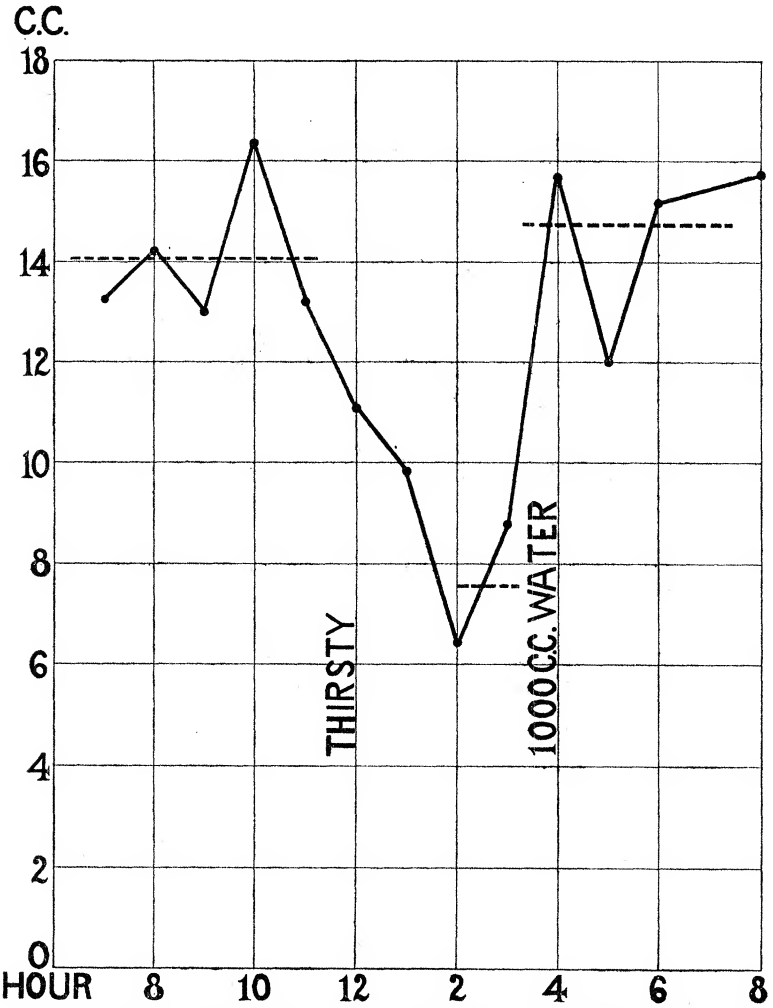

FIG. 1.—Chart showing saliva secreted each hour from 7 A.M. until 8 P.M. in consequence of chewing a tasteless gum five minutes. No fluid was drunk between 7 o'clock the previous evening and 3 o'clock P.M. For further description, see text.

of approximately 500 c.c. of body fluid as sweat was accompanied by a reduction in the salivary output of almost 50 per cent.

Corresponding to the diminution of the salivary output as the result of chewing was a diminution in the reflex flow as a consequence of letting the mouth become dry. The reflex flow has fallen, in my experience, from 3 or 4 c.c. in five minutes under normal conditions to a little more than 1 c.c. during thirst.

The relation between the decrease of salivary flow in these experiments and the sensation of thirst was quite definite. In the experiment illustrated in fig. 1, for example, the feeling of being "thirsty" was absent until the secretion of saliva began to decline, after 11 o'clock. From that time onward the back of the throat began to feel dry; there was frequent swallowing, and both the movements of the tongue and the act of deglutition were associated with a sense of "stickiness," a lack of adequate lubrication of the parts. All of this unpleasantness and discomfort disappeared after the restoration of the saliva flow by drinking water.

The increased spontaneous activity of the tongue and the repeated swallowing motions as "thirst" became more marked are noteworthy. These movements are a slight stimulus to salivary secretion, and they have, furthermore, the obvious effect of spreading about any fluid that might be present. In the absence of sufficient fluid, however, they augment the disagreeableness of the condition by making prominent the friction due to lack of lubricant. The "lump in the throat," which is complained of by persons who suffer from extreme thirst, can be explained as due to the difficulty encountered when the epiglottis and root of the tongue are rubbed over the dry back wall of the pharynx in attempts to swallow.

The only statement that I am aware of, which is contradictory to the evidence just presented, is that made by one of a group of psychologists, reported by Boring.* This one observer testified that when he was beginning to be thirsty the saliva flow was still copious. The eight other observers of the group speak of thirst as being characterised by dryness of the roof of the mouth, dryness of the lips, the sensation of having a "dry sore throat," feelings of stickiness, and uncomfortable "puckery" pressure localised in the middle and back of the tongue and in the palate—in other words, as one of them summed up his experience, "dryness expresses the complex as a whole." This body of testimony agrees closely with that presented earlier and suggests that there may have been error in the one observation that thirst was associated with free secretion of saliva.

Other evidence on the relation between absence of saliva and the presence of thirst as a sensation was obtained through checking salivary secretion by atropine. Before the injection the amount secreted during 5 minutes by chewing averaged 13·5 c.c. After the full effect of the drug was manifest, the amount fell to 1 c.c. All the feelings that were noted in ordinary thirst—the sense of dry surfaces, the stickiness of the moving parts, the difficulties of speaking and swallowing—all were present. These disagreeable experiences, constituting the thirst sensation, disappeared as soon as the mouth and throat

* Boring, 'The Psychological Review,' vol. 22, p. 307 (1915).

were washed out with a weak novocaine solution. The immediate effect in these circumstances was doubtless due to the water in the solution, but since the relief lasted much longer than when water was used, the anæsthetic was also a factor. This experience agrees with that of Lipidi-Chioti and Fubini, mentioned earlier. No water was drunk by me during the period of atropine effect, and yet when that effect disappeared, and the saliva flow was re-established, thirst also was abolished. The relation between thirst and such drug action has been noted before, but so strong has been the theory that thirst is a "general" sensation, that the drug has been supposed to produce its effect not by local action but by central changes and by alteration of the blood.*

Similar in character to the thirst which results from the action of atropine is that which accompanies anxiety and fright. The effect of such emotional states in causing inhibition of salivary secretion is well known. It was the basis of the ancient "ordeal of rice" employed in India as a means of detecting the guilty one in a group of suspected persons. It is illustrated in these days by Hoche's report of the effects of air raids on the people of Freiburg-in-Baden, in whom the signs of great fear—chattering of the teeth, pallor, and diarrhœa—were attended by intense thirst.† The unquenchable nature of the thirst which results from terror is a large part of the torment suffered by the novice in public speaking.

On the basis of the foregoing evidence I would explain thirst as due directly to what it seems to be due to—a relative drying of the mucosa of the mouth and pharynx. This may result either from excessive use of this passage for breathing, as in prolonged speaking or singing, or it may result from deficient salivary secretion. In the latter case "true thirst" exists, but it is not to be distinguished, so far as sensation is concerned, from "false thirst." True thirst is dependent on the fact that the salivary glands, which keep the buccal and pharyngeal mucosa moist, require water for their action. According to the observations and inferences of Wettendorff, the osmotic pressure of the blood is maintained, in spite of deprivation of water, by the withdrawal of water from the tissues. The salivary glands are included under "tissues," and they appear to suffer in a way which would support Wettendorff's view, for in the presence of a general need for water in the body, they fail to maintain the normal amount and quality‡ of secretion. The same is doubtless true of other glands. The importance of this failure of

* See Sherrington, 'Schäfer's Textbook of Physiology,' London, vol. 2 p. 991 (1900).

† Hoche, 'Med. Klinik,' vol. 13, p. 906 (1917).

‡ There is evidence that, as the quantity of saliva diminishes, its water content is less; *i.e.*, it is more viscous. (See Tezner, 'Arch. Intern. de Physiol.,' vol. 2, p. 153.)

action of the salivary glands, however, to the mechanism of the water supply of the body, lies in the strategic position of these glands in relation to a surface which tends to become dry by the passage of air over it. If this surface is not kept moist, discomfort arises and with it an impulse to seek well tried means of relief. Thus the diminishing activity of the salivary glands becomes a delicate indicator of the bodily demand for fluid.

The foregoing explanation is in agreement with the suggestions which have been offered to account for thirst as having a local origin. But it does not require specialised nerves, or peculiar sensitiveness of the first portion of the digestive tract, which have been assumed to be present by the upholders of this theory. And by calling attention to the arrangement by which the salivary glands are made to serve as indicators of the general bodily need for water, it presents a reasonable account of the manner in which a widespread condition of the organism may exhibit itself locally.

The experiments which have long been the chief support of the theory that thirst is a general sensation can also be explained by the evidence above adduced. The abolition of thirst by injecting fluid into the veins of thirsty animals would be expected, for, as shown in the experiment illustrated in fig. 1, by providing an adequate water supply the saliva flow is promptly re-established, and the parched mouth and throat are again continuously moistened. In the classic experiment of Claude Bernard the animal with an open gastric fistula continued to drink until the fistula was closed. This was not because there was a general demand for water throughout the body, so long as the fistula remained open, but because only when escape through the fistula was stopped did the body receive the water needed to provide the output of saliva which prevented local drying. And the dogs with salivary glands tied, described by Bidder and Schmidt, were always ready to drink, just as are persons who are terrified or who have been given atropine, because of thirst—because there is local drying of the mouth—from lack of saliva, though the body as a whole may not be in any need of water. The application of cocaine to the mucous surfaces of the mouth abolishes the torment of thirst, not by any central effect, and clearly not by satisfying any general bodily requirement for water, but by rendering the surfaces anæsthetic. The miraculous virtues of coca leaves, as a balm for the distress of the thirsty, a fact long ago observed, is explicable on these grounds. The thirst of those who suffer from loss of fluid from the body—the diabetic patient, the victim of cholera, the subject of hæmorrhage, the perspiring labourer, and the nursing mother—can be accounted for by the reduction of salivary flow as the water-content of the body is lowered, and by the consequent discomfort arising from the sticky buccal mucosa.

I am aware that many questions arising from the views which I have just developed remain to be solved—questions as to the effects which other glandular activity, removing fluid from the body, may exercise on the functions of the salivary glands; the alteration of properties of the blood and lymph other than osmotic pressure as affecting secretion; the relation between the so-called "free water" of the body fluids and salivary secretion when water is withheld; the influence of strong alcoholic beverages in producing thirst; and the nature of pathological states in which thirst seems to disappear. But these and other pertinent questions must await more peaceful times for their answers.

From the evidence presented, however, it seems to me that we are now in a position to understand the mechanisms by which all three of the essential supplies from the outer world are provided for in our bodily economy. The oxygen supply is arranged for by the control which changes in the blood, brought about mainly by variations in the carbon dioxide content, exert on the centre for respiration. The proper food supply ultimately is assured, because we avoid, or check, by taking food, the distressing pangs of hunger which powerful contractions of the empty stomach induce unless food is taken. And the water supply is maintained because we avoid, or abolish, by taking water or aqueous fluid, the disagreeable sensations which arise and torment us with increasing torment if the salivary glands, because of a lowering of the water-content of the body, lack the water they need to function, and fail therefore to pour out their watery secretion in sufficient amount and in proper quality to keep moist the mouth and pharynx.